DEPARTMENT OF THE ARMY
ARMED SERVICES BLOOD PROGRAM OFFICE
5109 LEESBURG PIKE
FALLS CHURCH, VA 22041-3258

REPLY TO
ATTENTION OF

ASBPO (40-2b)

BPL 03-01
7 January 2003

MEMORANDUM FOR SEE DISTRIBUTION

SUBJECT: Blood Donor Deferral for Smallpox Vaccination

1. The Armed Services Blood Program Office (ASBPO) was established by the Assistant Secretary of Defense for Health Affairs (ASD(HA)) to coordinate the blood programs of the Military Services and the Unified Commands. In that respect, the ASBPO is issuing Blood Program Letter (BPL) 03-01 notifying the Services of the policy regarding blood donor deferral and blood product quarantine and retrieval following smallpox vaccination (Enclosure 1).

2. The Food and Drug Administration (FDA) issued Final Guidance regarding the *Deferral of Donors and Quarantine and Retrieval of Blood and Blood Products in Recent Recipients of Smallpox Vaccine (Vaccinia Virus) and Certain Contacts of Smallpox Vaccine Recipients* (Enclosure 2) on 30 December 2002. This guidance was issued following President Bush's 16 December 2002 decision to begin a smallpox vaccination campaign targeted to those military and civilian personnel who have occupational risk of contracting smallpox. This guidance applies to collections of Whole Blood, blood components (including recovered plasma), Source Plasma and Source Leukocytes collected from allogeneic and autologous donors that is intended either for use in transfusion or for further manufacture into injectable products. These recommendations are applicable to pre-event, non-emergency smallpox vaccination and may be modified in the event of widespread emergency vaccination or due to an impending smallpox outbreak.

3. The smallpox vaccine is made from the vaccinia virus, a virus closely related to smallpox (variola virus). This vaccine is a live virus vaccine and as such, the smallpox vaccine poses a risk of transfusion-transmitted vaccinia infection. Therefore, recipients of the smallpox vaccine should be deferred from donation until transmission risk is abated. Enclosure 1 details specific donor deferral periods.

4. Vaccinia virus is readily recovered from the vaccination site until the vaccination scab spontaneously separates from the skin indicating healing. The scabs themselves contain infectious virus. Thus, although viremia is unlikely once an immune response is initiated, recipients of the vaccine could still inadvertently infect close contacts who touch the vaccination site or dressing, hence the FDA is extending deferrals to symptomatic close contacts of smallpox vaccine recipients.

5. **Service Blood Program Officers and Combatant Command Joint Blood Program Officers** must complete the enclosed form, *Acknowledgment of Receipt and Implementation*, (Enclosure 3) and return the signed original or fax copy to the ASBPO **NLT 10 January 2003.** A copy of all Service policy documents/letters implementing this BPL must also be forwarded to the within 30 days of implementation. The ASBPO point of contact for this action is Lt Col Ruth Sylvester. She can be reached at DSN 761-8011/8024, commercial (703) 681-8011/8024, or via e-mail at ruth.sylvester@otsg.amedd.army.mil.

G. MICHAEL FITZPATRICK
COL, USA, MSC
Director

3 Enclosures
as stated

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HEALTH AFFAIRS

JAN 0 9 2003

MEMORANDUM FOR SURGEON GENERAL OF THE ARMY
SURGEON GENERAL OF THE NAVY
SURGEON GENERAL OF THE AIR FORCE

SUBJECT: Blood Donor Deferral for Smallpox Vaccination

The Food and Drug Administration issued Final Guidance regarding the Deferral of Donors and Quarantine and Retrieval of Blood and Blood Products in Recipients of Smallpox Vaccine (Vaccinia Virus) and Certain Contacts of Smallpox Vaccine Recipients on 30 December 2002. The Armed Services Blood Program Office has coordinated and is issuing Blood Program Letter (BPL) 03-01, Blood Donor Deferral for Smallpox Vaccination, notifying the Services of this new blood donor deferral policy.

This policy is effective immediately and should be communicated to appropriate commanders, health care providers, and others involved in its implementation.

The point of contact for this matter is Colonel G. Michael Fitzpatrick, MS, USA, Director Armed Services Blood Program Office, at DSN 761-8024 or (703) 681-8024, glen.fitzpatrick@otsg.amedd.army.mil.

Ellen P. Embrey
Deputy Assistant Secretary of Defense
Force Health Protection and Readiness

SUBJECT: Blood Donor Deferral for Smallpox Vaccination

Purpose

Establish policy regarding blood donor deferral for recipients of smallpox vaccine and their close contacts who develop symptoms of vaccenia infection

- This policy applies to collections of Whole Blood, blood components (including recovered plasma), Source Plasma and Source Leukocytes collected from allogeneic and autologous donors that is intended either for use in transfusion or for further manufacture into injectable products.
- These requirements are applicable to pre-event, non-emergency smallpox vaccination and may be modified in the event of widespread emergency vaccination or due to an impending smallpox outbreak
- Services should update applicable Standardized Operating Procedures (SOP) IAW this policy.

Background

President Bush announced a decision on 16 December 2002 to start up vaccination against smallpox. The smallpox vaccine is a live virus vaccine made from the vaccinia virus, which is closely related to the smallpox virus, variola.

The smallpox vaccine currently being used is licensed by the Food and Drug Administration (FDA). The immune response to vaccinia includes neutralizing antibodies and a cellular immune response. Neutralizing antibodies are detected by 10 days after primary vaccination, reach peak levels around 2 weeks, and may persist for months to years. Cell mediated immunity to vaccinia can be detected after primary vaccination, and may persist for up to 50 years. There are no known cases of vaccinia virus persistence in the absence of a clinically recognizable infection.

Vaccinia virus is readily recovered from the vaccination site until the vaccination scab spontaneously separates from the skin. The scabs themselves contain infectious virus. Thus, although viremia is unlikely once an immune response is initiated, recipients of the vaccine could still inadvertently infect close contacts who touch the vaccination site or dressing. Persons infected following close contacts of vaccine recipients usually develop vaccinia lesions on their own skin following contact with vaccine site or contaminated material. Symptomatic close contacts pose the same risks as vaccination recipients.

The consequences of transfusion-transmitted vaccinia virus could include severe complications of vaccinia infection. Since the route of infection (intravenously vs. percutaneously) can influence the severity of complications, those transfusion recipients who are immunocompromised or who have burns or other serious skin conditions are at the greatest risk.

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Background (continued)

The inoculation of large numbers of individuals in a short period has the potential for an adverse impact on the nation's blood supply. Consequently, the FDA issued a Final Guidance document regarding the *Deferral of Donors and Quarantine and Retrieval of Blood and Blood Products in Recent Recipients of Smallpox Vaccine (Vaccinia Virus) and Certain Contacts of Smallpox Vaccine Recipients* on December 30, 2002.

Definitions

Close Contact is defined by the FDA as physical intimacy, touching of the vaccination site, touching of the bandages or covering of the vaccination site, or handling bedding or clothing that had been in contact with an unbandaged vaccination site.

Spontaneous separation of scab is defined by the FDA as occurring after the lesion has healed. The primary concern with the vaccination site is to ensure that it is completely healed, more than how the scab came off. A lesion is considered healed when there is no scab, exudates, bleeding, or opening. Healing is evidenced by pink, uninterrupted skin at the inoculation site. Attachment 1 provides pictorial of the expected response to the smallpox vaccine.

Complications of smallpox vaccination or inadvertent vaccinia infections include:

- Inadvertent inoculation at other sites (is the most frequent complication that occurs and the most common sites involved are the face, eyelid, nose, mouth, genitalia and rectum)
- Eczema vaccinatum
- Generalized vaccinia
- Progressive vaccinia
- Post-vaccinial encephalitis
- Vaccinial keratitis

Further information on complications of smallpox vaccination can be found at the Center for Disease Control and Prevention website http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5010a1.htm.

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Donor Screening

The following donor screening question will be asked of each allogeneic and autologous donor. This question will be added to the DD Form 572 as question 49 for the Allogeneic Question set and question 33 for the Autologous Question set. Follow-up questions will be asked for all donors answering YES to question 49/33.

<table>
<tr><th>Step</th><th>Action</th></tr>
<tr><td>1</td><td>Ask each donor, both allogeneic and autologous, the following question:</td></tr>
<tr><td></td><td>"In the past eight weeks, have you received a smallpox vaccination or have you had close contact with the vaccination site of anyone else?"</td></tr>
<tr><td>2</td><td>If the donor answers YES, ask the appropriate follow-up questions listed below:</td></tr>
<tr><td></td><td>
<table>
<tr><th>If the donor had ...</th><th>Then ask the donor...</th></tr>
<tr><td>A smallpox vaccination in the past 8 weeks</td><td>1. Has the vaccination scab fallen off your skin?
2. Did it fall off by itself?
3. Did you have any illness or complications due to the vaccination?</td></tr>
<tr><td>Close contact with a smallpox vaccination</td><td>Have you had any new skin rash or skin sore since the time of contact?</td></tr>
</table>
</td></tr>
</table>

NOTES:
1. Question 49/33 should be added to the DD Form 572.
2. The ASBPO MS Word file is located at http://www.tricare.osd.mil/asbpo/downloads/DD572_Jan03.doc
3. Follow-up questions should be asked orally and answers documented in Section V, Donor Medical History Comments, of the DD Form 572.

Continued on next page

Donor Deferral Donors will be deferred for smallpox vaccination in accordance with table below:

If the donor is a ...	And the ...	Then the donor is ...
Vaccine Recipient with no complications	scab spontaneously separated	**Deferred** ▪ until the scab separated ***OR*** ▪ 21 days after vaccination **WHICHEVER IS LATER** Must visually verify the absence of a scab and healing of the vaccination site prior to accepting the donor.
Vaccine Recipient-with no complications	scab **DID NOT** spontaneously separate	**Deferred** for 2 months from the date of vaccination
Vaccine Recipient-WITH complications		**Deferred** for 14 days after all vaccine complications have completely resolved
Close contact of a vaccine recipient	donor is asymptomatic (did not develop lesions or any other symptoms)	Not deferral
Close contact of a vaccine recipient and the donor developed localized skin lesions, with no other symptoms or complications	scab spontaneously separated	Not deferred Must visually verify the absence of a scab and healing of the lesion site prior to accepting the donor.
Close contact of a vaccine recipient and the donor developed localized skin lesions, with no other symptoms or complications	scab **DID NOT** spontaneously separate	**Deferred** for 2 months from date of attempted donation
Close contact of a vaccine recipient the donor developed complications		**Deferred** 14 days after all vaccine complications have completely resolved

Continued on next page

NOTES:

1. Document deferral in Section V, Donor Medical History Comments, of the DD Form 572 or in accordance with your Service specific SOP.
2. Use DBSS Deferral Code 206, Other Immunization and manually enter the appropriate return date.
3. Attachment 2 should replace page 4 of the Immunizations List (ASBPO BPL 02-04 Enclosure 2).
4. Attachment 3 should replace page 16 of the Medical Conditions list (ASBPO BPL 02-04, Enclosure 3).

Product Quarantine

Quarantine and retrieve previously collected in-date units of blood and blood components intended for transfusion, as well as unpooled units of Source Plasma, Source Leukocytes, and recovered plasma intended to make injectable products from donors who provide post-donation information that they had:

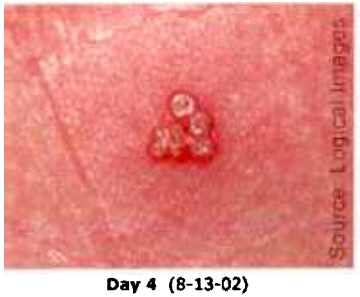
1.	Received a smallpox vaccination within 21 days before the donation
2.	A smallpox vaccination scab at the time of donation
3.	Symptoms or signs of vaccinia virus infection at the time of donation resulting from close contact with a recipient of smallpox vaccine
4.	A vaccinia complication within 14 days prior to donation; or
5.	A clinically apparent vaccinia virus infection during the 21 days after donation that may have resulted from contact prior to donation with a recipient of smallpox vaccine

Notification of Prior Transfusion Recipients

Medical directors should consider the need for prompt record tracing and, as appropriate, notification of the treating physicians or notification of prior recipients of the affected blood and blood components previously collected from donors who provide post-donation information that they had:

1.	Received a smallpox vaccination within 21 days before the donation
2.	A smallpox vaccination scab at the time of donation
3.	Symptoms or signs of vaccinia virus infection at the time of donation resulting from close contact with a recipient of smallpox vaccine
4.	A vaccinia complication within 14 days prior to donation; or
5.	A clinically apparent vaccinia virus infection during the 21 days after donation that may have resulted from contact prior to donation with a recipient of smallpox vaccine

Expected Response to Smallpox Vaccination



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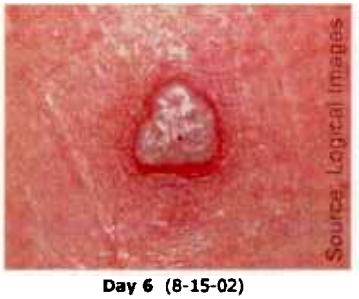
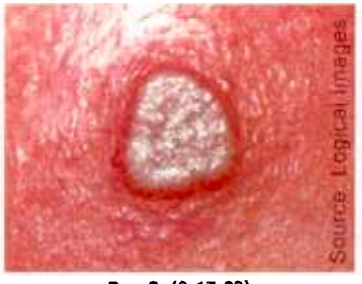
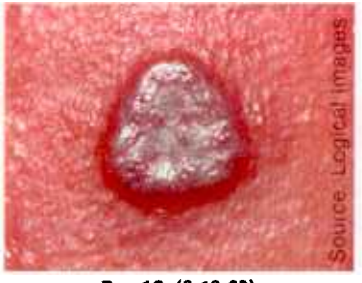


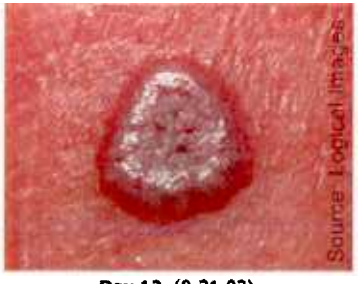
Day 6 (8-15-02)



Day 8 (8-17-02)



Day 10 (8-19-02)



Day 12 (8-21-02)

Day 14 (8-23-02)

Day 16 (8-25-02)

Day 18 (8-27-02)

Day 20 (8-29-02)

These would be considered “healed”
No Scab, exudate, bleeding or opening

Atch 1

Vaccine/Other Biologicals	Acceptibility	Note
Recombivax HB	Defer 1 day (may cause positive HbsAg due to antigen present in the vaccine). Defer 12 months if post-exposure.	Vaccine: Hepatitis B (Recombinant)
RhoGAM	Accept after pregnancy, miscarriage or abortion and meets required wait of 6 weeks.	Vaccine: Rh Immune Globulin
Rocky Mountain Spotted Fever vaccine	Accept immediately if symptom-free	
Rubella vaccine	Defer 4 weeks.	
Rubeola vaccine	Defer 2 weeks.	
Smallpox vaccine	Vaccinated donor, or donor who has a localized vaccinia lesion acquired through close contact with a vaccine recipient: --Defer until after the scab has separated from the skin spontaneously **or 21 days from date of immunization, *which ever is longer*.** as long as donor had no other symptoms or complications. --Visual verification of absence of vaccine scab is required. If scab was otherwise removed (**not spontaneously separated**) and: -- If donor is a **vaccine recipient**, defer for 2 months after vaccination date. -- If donor had localized lesion acquired through **close contact** with a vaccine recipient, defer for 2 months after the date of attempted donation, as long as donor had no other symptoms or complications. If donor experienced complications of vaccinia infection acquired either through vaccination or close contact with vaccine recipient, defer until 14 days after all complications are completely resolved.	Vaccine: Vaccinia virus (from cowpox) closely related to smallpox provides protective immunization to smallpox. Close contact: Touching the vaccination site, touching the bandages or covering of the vaccination site, or handling clothing that had been in contact with an ***unbandaged*** vaccination site.
Tetanus vaccine	Accept immediately if symptom-free	
Tetramune	Accept immediately if symptom-free.	Vaccine: Diphtheria, Tetanus Toxoids, Pertussis, and Haemophilus b Conjugate
Tice BCG, USP	If given to treat cancer, permanent deferral. If given for tuberculosis exposure or prevention, defer 2 weeks if asymptomatic and donor meets medical criteria for tuberculosis.	Vaccine: Live culture preparation of the Bacillus of Calmette and Guerin (BCG) strain MYCOBACTERIUM BOVIS
Tri-Immunol Adsorbed	Accept immediately if symptom-free.	Vaccine: Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed
Tripedia	Accept immediately if symptom-free.	Vaccine: Diphtheria and Tetanus Toxoids and Pertussis Vaccine Adsorbed

MEDICAL CONDITION	COMMENT
Rubella (German Measles)	Defer 1 month after exposure unless immunization or previous infection can be documented.
Salmonella	Defer until well and released from doctor's care. Permanent deferral if recurrent septicemia.
Sarcoidosis	Permanent deferral if systemic, accept if limited.
Scabies	Defer until resolved.
Scarlet Fever	Accept if well and asymptomatic. If heart disease see Rheumatic Heart Disease. If exposed to patient, defer until 48 hours after exposure and well.
Scarring	Intentional skin scarring to make a design: 12 month deferral
Schizophrenia	Accept if donor is mentally and legally responsible.
Scleroderma	Permanent deferral.
Seizures	See Convulsions.
Sepsis	Accept if no longer on antibiotics for 1 week and condition resolved.
Shigella	Accept if resolved or asymptomatic.
Shingles	Defer while active lesions present and for 1 week afterwards. Accept when lesions inactive.
Shortness Of Breath	Shortness of breath on exertion is acceptable, providing donor is active and has no restrictions on his/her activities
Sickle Cell Disease	Permanent deferral.
Sickle Cell Trait	Accept.
Sinusitis	Accept unless being treated with antibiotics, then defer until course completed and feels well.
Sjogren's Syndrome	Permanent deferral.
Skin Infections	Accept if lesions not in area of venipuncture and donor not taking antibiotics. [If suspect for anthrax, defer.]
Skin ulcer	Defer until well-healed. [If suspect for anthrax, defer.]
SLE (Systemic Lupus Erythematosus)	Permanent deferral.
Smallpox lesion	Permanent deferral, unless vaccinated donor or donor with localized vaccinia lesion acquired through close contact with a vaccine recipient. Defer until after the scab has separated from the skin spontaneously or 21 days after date of immunization *which ever is longer*, as long as no other symptoms or complications. If scab was otherwise removed; defer vaccine recipient for 2 months after vaccination date, defer donors with localized/close contact lesion for 2 months after date of attempted donation, as long as no other symptoms or complications.
Smallpox vaccination complications	Defer any donor who experienced complications of vaccinia infection acquired either through vaccination or through close contact with vaccine recipient until 14 days after all complications are completely resolved

Guidance for Industry

Recommendations for Deferral of Donors and Quarantine and Retrieval of Blood and Blood Products in Recent Recipients of Smallpox Vaccine (Vaccinia Virus) and Certain Contacts of Smallpox Vaccine Recipients

FINAL GUIDANCE

This guidance is being distributed for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.115(g)(3) without initially seeking prior comment because the agency has determined that prior public participation is not feasible or appropriate. FDA made this determination because vaccination programs may start soon, and blood establishments need to clarify the suitability of donors who have been recently vaccinated or who have been infected through close contact with a recently vaccinated person. FDA invites comments on this document. Please submit comments to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. You should identify all comments with the docket number listed in the notice of availability that published in the *Federal Register*. FDA will review any comments we receive and revise the guidance document when appropriate.

Additional copies of this guidance are available from the Office of Communication, Training and Manufacturers Assistance (HFM-40), 1401 Rockville Pike, Rockville, MD 20852-1448, or by calling 1-800-835-4709 or (301) 827-1800, or from the Internet at http://www.fda.gov/cber/guidelines.htm.

For questions on the content of this guidance contact the Division of Blood Applications, Office of Blood Research and Review at (301) 827-3543.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research (CBER)
December 2002

Table of Contents

GUIDANCE FOR INDUSTRY

Recommendations for Deferral of Donors and Quarantine and Retrieval of Blood and Blood Products in Recent Recipients of Smallpox Vaccine (Vaccinia Virus) and Certain Contacts of Smallpox Vaccine Recipients

This guidance document represents the agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternate approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

I. INTRODUCTION

This guidance document provides the current recommendations of the Food and Drug Administration (FDA) for assessment of donor suitability and quarantine and retrieval of blood and blood products in cases of donors exposed to vaccinia virus, which is the virus used in smallpox vaccines. The presence of vaccinia virus in transfused blood or plasma could be harmful to some recipients. Although the presence of vaccinia virus in blood (viremia) has rarely been documented, this possibility has not been assessed using modern laboratory techniques. Therefore, the risk of transmission of vaccinia virus by blood and blood products is uncertain.

Because of the likelihood of vaccination of many people with the smallpox vaccine, we are issuing guidance on measures to reduce any possible risk of transmission of vaccinia virus from donors of blood and blood products.

This guidance applies to collections of Whole Blood, blood components (including recovered plasma), Source Leukocytes, and Source Plasma intended for use in transfusion or for further manufacturing into injectable products. FDA developed the recommendations in this guidance in consultation with experts on vaccinia virus at the Centers for Disease Control and Prevention (CDC) and at the Department of Defense. This document is intended to provide guidance pertaining to pre-event, non-emergency, smallpox vaccination. In the event of widespread emergency vaccination due to an actual or impending smallpox outbreak, the risk-benefit evaluation may change, and these recommendations for donor deferrals, and for product quarantine and retrieval, may need to be modified according to the circumstances and available scientific information.

Throughout these recommendations, "you" refers to blood and plasma collection establishments. FDA uses mandatory language, such as "shall," "must" and "require," when referring to statutory or regulatory requirements. We use non-mandatory language, such as "should," "may," "can," and "recommend" when referring to recommendations.

II. BACKGROUND

Vaccinia virus, a virus related to cowpox virus, is a double-stranded DNA virus, which has been used to vaccinate against smallpox for more than 100 years. Because vaccinia virus and smallpox (variola virus) are closely related, the immune response to vaccinia is protective against smallpox. All modern smallpox vaccines are live virus vaccines comprised of vaccinia virus, and smallpox vaccines in the U.S. are derived from the New York City Board of Health (NYCBOH) strain of vaccinia virus.

Smallpox vaccination was routinely performed in the U.S. until 1971. In recent years, smallpox vaccination has been recommended only for laboratory personnel working with certain orthopoxviruses, including vaccinia and smallpox. On June 20, 2002, the Advisory Committee for Immunization Practices (ACIP) of the CDC recommended that smallpox vaccine also be given to persons pre-designated to conduct investigation and follow-up of initial smallpox cases and to personnel in facilities that are pre-designated to serve as referral centers to provide care for initial smallpox cases (www.cdc.gov/nip/smallpox/supp_recs.htm). On December 13, 2002, President Bush announced his decision to begin a smallpox vaccination campaign targeted to those military and civilian personnel who have an occupational risk of contracting smallpox.

During the first stage, States will provide smallpox vaccination on a voluntary basis to those public health and health care workers who are most likely to be exposed to the first cases during a smallpox outbreak. Approximately 500,000 individuals will be eligible to receive the vaccine during this stage. During the second stage, States will provide smallpox vaccination, also on a voluntary basis, to other health care workers, emergency medical personnel, ambulance drivers, firemen, policemen, and others who may encounter smallpox cases in the course of their duties. Approximately 10 million individuals will be eligible to receive the vaccine during this stage. Although the U. S. Government does not recommend smallpox vaccination for members of the general public at this time, the President has directed the Health and Human Services (HHS) and its public health partners to develop means to accommodate those members of the general public who, despite these current recommendations, seek to obtain access to vaccination before a new licensed vaccine is available.

Smallpox vaccine is administered percutaneously. A papule forms 3-5 days after a primary vaccination (no prior vaccination) and subsequently becomes a vesicle. The vesicle then becomes pustular, reaching its maximum size at 8-10 days. The scab that forms usually separates from the skin 14-21 days after vaccination, but it may persist for up to 6 weeks (Ref. 1). Two different investigators, in 1930 and 1953, reported that vaccinia virus could sometimes be isolated from the patient's blood 3-10 days after vaccination (Ref. 2). These studies did not use the less virulent NYCBOH strain of vaccinia virus that comprises currently available vaccines in the U.S. Using the NYCBOH strain of vaccinia virus, other investigators were only able to detect virus in the blood of patients with disseminated infection, but never in patients who only had localized lesions (Refs. 3,4). All of these studies are of limited value because of their small size. Studies are now underway to determine the presence and frequency of vaccinia virus in the blood after vaccination.

The consequences of transfusion-transmitted vaccinia virus could include severe complications of vaccinia infection. These would be particularly likely in transfusion recipients who are immunocompromised or who have burns, or other serious skin conditions. In addition, vaccinia virus infection rarely can cause severe complications such as encephalitis and severe generalized vaccinia in otherwise healthy people. It is possible that vaccinia infection transmitted intravenously would result in different or more severe infections than when acquired percutaneously, since the route of infection can influence the severity (Ref. 5).

III. RATIONALE FOR DONOR DEFERRAL AND PRODUCT QUARANTINE

A. Rationale for Deferral of Recipients of Smallpox Vaccine

The immune response to vaccinia includes neutralizing antibodies and a cellular immune response. Neutralizing antibodies are detected by 10 days after primary vaccination, reach peak levels around 2 weeks, and may persist for months to years (Refs. 6,7). Cell mediated immunity to vaccinia can be detected after primary vaccination, and may persist for up to 50 years (Refs. 8,9). There are no known cases of vaccinia virus persistence in the absence of a clinically recognizable infection.

Vaccinia virus is readily recovered from the vaccination site until the vaccination scab spontaneously separates from the skin. The scabs themselves contain infectious virus. Thus, although viremia is unlikely once an immune response is initiated, recipients of the vaccine could still inadvertently infect close contacts who touch the vaccination site or dressing (Ref. 10). Vaccinia virus can be recovered from the skin at the vaccination site for a mean duration of 7.8 days, with a range of 0 to 18 days (Ref. 11). Based on these considerations, and until more information is available, we recommend that you defer donors who received smallpox vaccine until after the vaccine scab has spontaneously separated (see section IV.). We will continue to evaluate our recommendations in light of evolving scientific knowledge about vaccinia virus.

B. Rationale for Deferral of Donors with Complications of Smallpox Vaccination

Viremia has been more readily detected in people with moderate or severe complications of vaccinia virus infection (Ref. 3). These complications include generalized vaccinia, eczema vaccinatum, and progressive vaccinia. The occurrence of viremia in cases of encephalitis or vaccinial keratitis has not been demonstrated. To assure a margin of safety, we recommend that you defer donors with complications of vaccinia (as defined in the Appendix), acquired by vaccination for 14 days after complete resolution of the complication, as stated in section IV., below.

C. Rationale Concerning Asymptomatic Contacts of Vaccine Recipients

Asymptomatic contacts of vaccinees are unlikely to be infected and we do not recommend that they be deferred.

D. Rationale for Deferral of Donors Who Have Contracted Symptomatic Vaccinia Virus Infection through Close Contact with a Vaccine Recipient

Persons infected by close contact with a vaccine recipient (Ref. 10) usually develop vaccinia lesions on their own skin, since the virus is transmitted to them by skin contact with the vaccination site or with other parts of the body or clothing that has been recently contaminated with vaccinia virus. As stated in section IV., below, you should defer donors who have had contact with someone else who has received the vaccine only in cases where the donors have recognizable signs or symptoms attributable to the virus. These donors present the same risks to blood recipients and collection center staff as someone who has been recently vaccinated. However, donors who have been exposed to a vaccinee, but who fail to develop signs or symptoms of infection by vaccinia, are unlikely to be infected. If infected donors have a single, localized lesion, we recommend that they be deferred until the scab has spontaneously separated. In cases where the scab was otherwise removed, we recommend deferral periods based on the date of vaccination of the vaccine recipient. As with smallpox vaccine recipients (section III. B., above), if the contacts have complications of their vaccinia virus infection, we recommend that they be deferred until 14 days after all complications have completely resolved.

E. Rationale for Product Quarantine

Vaccinia virus in blood and blood products could pose a risk to transfusion recipients of severe complications of vaccinia infection. For this reason, you should quarantine blood and blood products that were collected from donors identified as having vaccinia virus infection as stated in section IV., below. Pooled plasma for further fractionation, or products made from that pooled plasma, need not be quarantined because the manufacturing process and virus inactivation procedures applied to them are believed to be adequate to eliminate infectious vaccinia virus from the final product (Refs. 12-14).

There is no need to discard plasma that has been quarantined provided it is labeled for use in the manufacture of non-injectable products or for research use only, since such products represent minimal or no risk to the health of users.

IV. RECOMMENDATIONS FOR DONOR DEFERRAL

Consistent with existing regulations and applicable guidance, donors should be in good health and free of acute respiratory illnesses and of infectious skin disease presenting a risk of contamination of the blood and plasma. [21 CFR 640.3(b)(4),(5) and 21 CFR 640.63(c)(7),(8)] Furthermore, donors must be free from disease transmissible by blood transfusion, insofar as can be determined by history and examinations [21 CFR 640.3(b)(6) and 21 CFR 640.63(c)(9)]. Blood and plasma collection establishments should try to identify potential donors who have recently received smallpox vaccine; to identify such donors, we recommend that you ask the questions described below in the donor questionnaire. Standard operating procedures that are already in place should allow identification of donors who have had complications of smallpox vaccination, or who have contracted localized infection or complications of vaccinia infection from exposure to a vaccine recipient. For donors who state that they have been vaccinated

within the past two months, collection center staff should visually inspect the site of the vaccination (usually on the upper arm) to determine whether the scab has separated from the skin, and if there has been recent vaccination we recommend that they inquire whether the scab separated spontaneously. We recommend that all donors be asked the following questions:

A. Donor Deferral Questions

1. "In the past eight weeks, have you received smallpox vaccination or have you had close contact with the vaccination site of anyone else?." [Examples of close contact include physical intimacy touching the vaccination site, touching the bandages or covering of the vaccination site, or handling bedding or clothing that had been in contact with an unbandaged vaccination site.]

    a. [If the donor had smallpox vaccination:] Has the vaccination scab fallen off your skin by itself? Did you have any illness or complications due to the vaccination?
    b. [If close contacts had smallpox vaccination:] Have you had any new skin rash or skin sore since the time of contact?

B. Deferral of Recipients of Smallpox Vaccine

The following recommendations apply to donors who recently have received smallpox vaccine, as identified by donor questioning. [As noted on the first page of this guidance, in the event of widespread emergency vaccination, the deferral recommendations for vaccinated individuals may need to be modified according to the circumstances and available scientific information.]

Donors without vaccine complications (as defined in Appendix):

Donors without vaccine complications should be deferred until after the vaccination scab has separated spontaneously, or for 21 days post-vaccination, whichever is the later date. Donor room staff should visually verify absence of the vaccination scab and ask if it separated spontaneously. In cases where a scab was removed prior to separating spontaneously, we recommend that you defer the donor for two months after vaccination.

2. Donors with vaccine complications (as defined in Appendix):

We recommend that you defer donors who have experienced complications of vaccination until 14 days after all vaccine complications have completely resolved.

C. Deferral of Symptomatic Contacts of Recipients of Smallpox Vaccine

The following recommendations apply to donors who acquired a clinically recognizable vaccinia virus infection by close contact with someone who received the smallpox vaccine.

Donors with localized skin lesions and without any other symptoms or complications:

Donor room staff should visually verify the absence of the localized skin lesion (scab) and ask if it separated spontaneously. If the localized skin lesion (scab) separated spontaneously, and is no longer present, the donor need not be deferred based on the prior exposure to a smallpox vaccine recipient. In cases where a scab was otherwise removed, we recommend that the donor be deferred for a period of three months from the date of the vaccine recipient with whom the contact occurred. If the date is not known, but could have been within the last three months, we recommend that you defer the donor for two months from the present time.

2. Donors with vaccinia complications (as defined in Appendix):

We recommend that you defer donors who have experienced complications of vaccinia infection acquired through close contact with a vaccine recipient until 14 days after all vaccine complications have completely resolved.

V. RECOMMENDATIONS FOR PRODUCT QUARANTINE AND RETRIEVAL

We recommend that you quarantine and retrieve from consignees the relevant previously collected in-date units of blood and blood components intended for transfusion, as well as unpooled units of Source Plasma, Source Leukocytes, and recovered plasma intended to make injectable products, if you receive post-donation information that a donor had:

1) received a smallpox vaccination within 21 days before the donation,
2) a smallpox vaccination scab at the time of donation,
3) symptoms or signs of vaccinia virus infection at the time of donation resulting from close contact with a recipient of smallpox vaccine,
4) a vaccinia complication within 14 days prior to donation, or
5) a clinically apparent vaccinia virus infection during the 21 days after donation that may have resulted from contact prior to donation with a recipient of smallpox vaccine.

These units placed in quarantine should be labeled and used only for manufacture of non-injectable products or for research use; otherwise they should be destroyed.

VI. RECOMMENDATIONS FOR NOTIFICATION OF PRIOR TRANSFUSION RECIPIENTS

In the case that subsequent to donation, a donor is reported to have:

1) received a smallpox vaccination within 21 days before the donation,
2) a smallpox vaccination scab at the time of donation,
3) symptoms or signs of vaccinia virus infection at the time of donation resulting from prior contact with a recipient of smallpox vaccine,
4) a vaccinia complication within 14 days prior to donation, or
5) a clinically apparent vaccinia virus infection during the 21 days after donation that may have resulted from close contact prior to donation with a recipient of smallpox vaccine;

we recommend that medical directors consider the need for prompt record tracing and, as appropriate, notification of the treating physicians or notification of prior recipients of the affected blood and blood components previously collected from that donor.

VII. IMPLEMENTATION

We recommend that you implement the recommendations in this guidance immediately. Under 21 CFR 601.12, licensed establishments implementing these recommendations should submit by official correspondence a statement in their annual reports indicating the date that the establishment revised standard operating procedures to implement these recommendations.

VIII. REFERENCES

1. Fenner, F., et al. Smallpox and its eradication, page 140; available at www.who.int/emc/diseases/smallpox/smallpoxeradication.html.

ibid.

3. Blattner, R.J. et al, Antibody response to cutaneous inoculation with vaccinia virus: viremia and viruria in vaccinated children. J. Pediatr.. 64: 839-52, 1964.

4. Kempe, CH., Studies on smallpox and complications of smallpox vaccination. Pediatrics 26:176-89, 1960.

5. Fenner, op.cit. p. 122-124.

6. Fenner, op.cit. p. 158.

7. Stienlauf, S. et al, Kinetics of formation of neutralizing antibodies against vaccinia virus following revaccination, Vaccine 7: 201-4, 1999.

8. Ennis, F.A. et al. Primary induction of human CD8+ cytotoxic T lymphocytes and interferon-gamma producing T cells after smallpox vaccination. J. Infect. Dis. 185: 1657-9, 2002.

9. Demkowicz, WE.Human cytotoxic T-cell memory: long-lived responses to vaccinia virus. J. of Virology 70: 2627-31, 1996.

10. Morbid. Mortal. Weekly Report: Recommendations and Reports (50/RR10): -25, June 22, 2001. at www.cdc.gov/mmwr/preview/mmwrhtml/rr5010a1.htm.

11. Koplan, JP and Martens KM.Smallpox vaccination revisited. Am. J. Trop. Med. Hygiene 24: 656-63, 1974.

12. Uemura, Y., et al, Inactivation and elimination of viruses during preparation of human intravenous immune globulin, Vox Sang 67:246-54, 1994.

13. Reid, KG et al, Potential contribution of mild pepsin treatment at pH4 to the viral safety of human immune globulin products, Vox Sang 55:75-80, 1988.

14. Uemura, Y et al, Inactivation and elimination of viruses during the fractionation of an intravenous immune globulin preparation: liquid heat treatment and polyethylene glycol fractionation, Vox Sang 56:155-61, 1989.

15. Goldstein, J.A . et al. Smallpox vaccination reactions, prophylaxis, and therapy of complications. Pediatrics 55(3): 342-47, 1975.

IX. APPENDIX: MODERATE AND SEVERE COMPLICATIONS OF SMALLPOX VACCINATION AND INADVERTENT VACCINIA VIRUS INFECTION

Complications of smallpox vaccine or of inadvertent vaccinia virus infection, for the purpose of this guidance, are defined as the following, and are consistent with CDC definitions of moderate to severe adverse reactions to the smallpox vaccine, or to inadvertent vaccinia virus infection in contacts of vaccine recipients (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5010a1.htm).

1. Eczema vaccinatum
2. Generalized vaccinia
3. Progressive vaccinia
4. Postvaccinial encephalitis
5. Vaccinial keratitis

Eczema vaccinatum is a localized or systemic dissemination of vaccinia virus in someone with eczema (atopic dermatitis) or a history thereof, or with other chronic or exfoliative skin conditions.

Generalized vaccinia is characterized by a vesicular rash of varying extent that can occur among persons without underlying illnesses. The rash is generally self-limited and requires minor or no therapy except in rare cases, when the vaccine recipient is systemically ill.

Progressive vaccinia (vaccinia necrosum) is a severe, potentially fatal illness characterized by progressive necrosis in the area of vaccination, often with metastatic vaccinia lesions. It has occurred almost exclusively among persons with cellular immunodeficiency.

Postvaccinial encephalitis is a rare but serious complication of vaccinia virus infection.

Vaccinial keratitis is an infection of the cornea, which can cause corneal scarring and visual impairment. This condition is usually caused by accidental self-inoculation of the eye from the vaccine site, or from self-inoculation after contact with another vaccine recipient, and is not believed to be due to hematogenous spread or associated with a secondary viremia (Ref. 15).

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BPL 03-01

Blood Donor Deferral for Smallpox Vaccination

7 January 2003

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